REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1-7 were pending in this application when last examined.

Claims 1-7 were examined on the merits and stand rejected.

Claims 3, 4, 6 and 7 are amended to clarify the claimed invention.

No new matter has been added.

II. INDEFINITENESS REJECTION

On page 2 of the Office Action, claims 3-4 and 6-7 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons set forth. This rejection is overcome, as applied to the amended claims, for reasons which are self-evident.

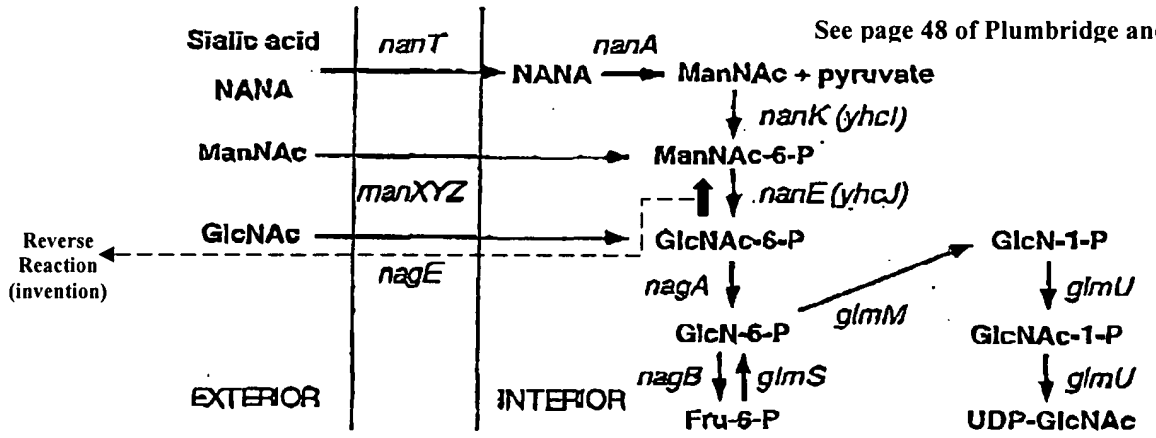
III. OBVIOUSNESS REJECTION

On page 3 of the Office Action, claims 1-7 were rejected under 35 U.S.C. § 103 as unpatentable over Koizumi et al., U.S. 2002/0064836, in view of Plumbridge and Vimr, and further in view of Ishige et al. and Tabata et al.

Applicants respectfully traverse this rejection as applied to the amended claims.

Plumbridge and Vimr performed a gene disruption experiment on *E. coli* and predicted on the basis of their results that the enzyme GlcNAc-6P-2-epimerase is encoded by *nanE* gene (see page 52, middle portion in the right column). However, they did not actually confirm the enzyme activity by inducing expression of the enzyme. Moreover, according to this article, the enzyme encoded by *nanE* was predicted to catalyze the reaction ManNAc-6-P → GlcNAc-6P in the metabolic pathway of ManNAc. We wish to draw the Office's attention to the fact that this is the reverse reaction (see the figure below) to that employed in the claimed invention. Knowing that a reaction from ManNAc-6-P → GlcNAc-6P proceeds, those skilled in the art cannot immediately tell whether the reverse reaction GlcNAc-6P → ManNAc-6-P in fact proceeds. On the other hand, the present inventors actually constructed a system for producing

this enzyme, GlcNAc-6P-2-epimerase, and actually confirmed the availability of the reaction of GlcNAc-6-P → ManNAc-6-P.



Thus, this reference fails to teach or suggest GlcNAc-6-P → ManNAc-6-P by GlcNAc-6P-2-epimerase.

On the other hand, in "Enzyme and Microbial Technology" GlcNAc is used as a substrate, and GlcNAc 2-epimerase is utilized in *E. coli* cells. In this case, when GlcNAc is taken up by *E. coli* cells, the phosphotransferase system acts on GlcNAc and transforms it into GlcNAc-6P. Therefore, as described in the specification (see pages 3-4), use of GlcNAc-6P-2-epimerase is considered more efficient and beneficial, because if GlcNAc 2-epimerase is employed, an amount of GlcNAc that had been transformed into GlcNAc-6P can no longer be used by the reaction, resulting in a reduction in yield. In addition, since GlcNAc 2-epimerase requires ATP for exhibiting its activity, this reference utilizes ATP present in *E. coli* cells. However, this approach has a drawback in that sufficient amounts of ATP are not available, and such an insufficient ATP supply is also considered to be a factor that contributes to a reduction in yield.

Thus, according to the data provided in this article (see page 331), 800 mM GlcNAc produced 39.7 mM NeuAc (yield: 5%). In contrast, according to the claimed invention (see the specification, pages 20-21), 100 nM GlcNAc produced 43.7 mM NeuAc (yield: 44%). This is a significant improvement not taught or suggested by the cited art.

Further, the claimed invention is directed to a process for producing CMP-NeuAc from inexpensive raw material. To reduce the cost, the inventive process makes use of enzyme's

ability to phosphorylate CMP, and uses it as a CTP supply source. Applicants note there are other microorganism species that transform CMP into CTP. Among various microorganisms the present inventors had tested in the reaction scheme of the present application, yeast provided the highest CMP-NeuAc yield. That is why yeast is mentioned in the present invention. In other words, it is old knowledge that a variety of microorganisms, including yeast, have ability to transform CMP to CTP. Therefore, the Office's reliance on Biosci. Biotechnol. Biochem., Vol 65, 1736-1740, 2001 to reject the claimed invention is misguided. Applicants have shown yeast provide high CMP-NeuAc yield.

Further, the claimed invention utilizing dry yeast in a system that supplies CTP and PEP simultaneously is novel, because in the synthesis process making use of NeuAc synthase, dry yeast plays two roles; supplying CTP and serving as a PEP supply source.

Thus, the noted references fail to render obvious the claimed invention because (1) Plumbridge and Vimr teach a reverse reaction than the one employed in the present invention and therefore do not provide enabling disclosure for the present invention, (2) the cited references fail to teach the significantly improved efficiency of the claimed invention, (3) the claimed invention is directed towards a process for producing CMP-NeuAc from inexpensive raw materials not suggested by the prior art, (4) Applicants have shown yeast provide high CMP-NeuAc yield and (5) the claimed invention uses dry yeast to supply CTP and to serve as PEP supply source.

Thus, for the above-noted reasons, this rejection as applied to the amended claims is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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July 31, 2008